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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	4

DATE MAILED: 07/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)	
09/732,754	DRUILHE ET AL.	
Examiner	**Art Unit**	
Maher M. Haddad	1644	

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,15,20-24 and 26-40* is/are pending in the application.

4a) Of the above claim(s) *1-9,15 and 20-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

1. Claims 1-9, 15, 20-24 and 26-40 are pending.

2. Claims 1-9, 15, and 20-24 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

3. Claims 26-40 are under consideration in the instant application.

4. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/5/03 has been entered.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> *The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.*

6. Claims 26-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising a lipoprotein of SEQ ID NOS: 1- 3 for *in vivo* induction of both B- and T-cell responses, does not reasonably provide enablement for any other composition consisting essentially of any lipopeptide "comprising" a sequence of SEQ ID NO: 2 or SEQ ID NO: 3, capable of inducing an immune systemic response specific to said sequence with administered via a mucosal rout without adjuvant in claims 26 and 30 wherein said lipopeptides has at least any lipid residue bound to an epitope T amino acid sequence and optionally at least one epitope B amino acid sequence in claims 27 and 31; any vaccine composition for mucosal administration comprising the composition of claim 26/30, which induces a B and/or T cell response in vivo in the absence of an adjuvant in claims 28 and 32, or any immunogenic composition comprising the composition of claim 26/30 in claims 29 and 30, wherein the immune systemic response is a systemic B and T cell response specific to said peptide and wherein the immune systemic response is stronger than immune systemic response induced when said peptide is administered by parenteral rout in claim 34, wherein the mucosal rout is intranasal route in claims 35 and 38, wherein the mucosal route is sublingual route in claims 36 and 39, wherein said immune response induces a mucosal protection in vivo against a malaria infection in claims 37 and 40. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The term "comprising" in claims 26 and 30 is open-ended, it would open up the claims to include unrecited amino acids on either or both of the N- or C- termini of given sequence. These additional amino acids significantly interfere with the activity of the lipopeptide.
For instance, the length of the peptide is important for binding to HLA (along with the presence of anchor (or "motif") amino acid residues present within the peptide). The peptides that bind to class I molecules have a predominant length. A primary factor for this is that amino acid residues at the amino- and carboxy-termini of peptides binding to class I molecules interact with conserved amino acid residues in pockets ("A","F") located at opposite ends of the binding groove of the class I molecule, giving rise to a common orientation of the peptides in the binding site (Engelhard at page 14, column 1, lines 16-27.) Thus, the amino acid residues at the peptides' termini make a network of hydrogen bonds with conserved residues on the sides and bottom of the peptide binding groove of class I molecules. These interactions are important for holding the peptides in the binding groove and for stabilizing the complex (Guo, et al at page 366, column 1 lines 1-10.) "...the preferred length (of the peptide) is determined by the minimum amount of peptide required to span the center of the binding site and optimize the interactions at the ends." (Engelhard at page 14, column 1, lines 23-27.) The minimum amount of peptide required to span the binding groove and make favorable contacts with their N-and C-termini may be dependent upon the sequence of the peptide itself since different amino acid residues have different physicochemical properties, and may be dependent upon the identity of the additional amino acids, since these residues may make a negative contribution to binding. Accordingly, there is a high level of unpredictability in designing/selecting longer sequences that would still maintain binding function, and applicant does not provide direction or guidance to do so.

The goal of vaccination is the induction of circulating specific antibodies to prevent the initial infection of the liver with the parasite. There is no sufficient guidance provided to assist one skilled in the art in the selection of all such possible vaccine containing any lipopeptide nor is there evidence provided that any lipoprotein or lipopeptide would be therapeutically effective. It appears that undue experimentation would be required of one skilled in the art to practice the claimed composition in providing effective vaccines to induce the circulating parasite specific antibodies.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the

unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

7. Claims 26-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of SEQ ID NOS: 1- 3 for the induction of B- and T- cell responses.

Applicant is not in possession of any composition consisting essentially of any lipopeptide "comprising" a sequence of SEQ ID NO: 2 or SEQ ID NO: 3, capable of inducing an immune systemic response specific to said sequence with administered via a mucosal rout without adjuvant in claims 26 and 30 wherein said lipopeptides has at least any lipid residue bound to an epitope T amino acid sequence and optionally at least one epitope B amino acid sequence in claims 27 and 31; any vaccine composition for mucosal administration comprising the composition of claim 26/30, which induces a B and/or T cell response in vivo in the absence of an adjuvant in claims 28 and 32, or any immunogenic composition comprising the composition of claim 26/30 in claims 29 and 30, wherein the immune systemic response is a systemic B and T cell response specific to said peptide and wherein the immune systemic response is stronger than immune systemic response induced when said peptide is administered by parenteral rout in claim 34, wherein the mucosal rout is intranasal route in claims 35 and 38, wherein the mucosal route is sublingual route in claims 36 and 39, wherein said immune response induces a mucosal protection in vivo against a malaria infection in claims 37 and 40.

The term "comprising" means that a compound can include additional amino acids on either or both of the N- or C- termini of given sequence. Applicant has disclosed only SEQ ID NOS: 1-3; therefore, the skilled artisan cannot envision all the contemplated amino acid sequence possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant submits the rejection is obviated by replacing the term "having" with the more conventional term "comprising". Applicant argues that as search on USPTO web-site for the years 1976-present reveals 177 patents that have issued with the phrase "comprising the sequence of SEQ ID NO:". Applicant indicated that Applicants do not agree with the Examiner's assertion that the Applicant is not in possession of any other composition than those consisting of tailed-lipid peptides referring to sequences SEQ ID NOs:1-3, nor when the Examiner asserts that conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred. Applicant submits that BenMohamed et al (Eur. J. Immunol. 2002, 32:2274-2281) in which the inventors/authors disclose that they were able to induce systemic immune response with other antigens and in accordance with the present specification in that "lipopeptides derived from herpes and cytomegalovirus showing that this mode of mucosal immunization extends to other antigens".

However, the Examiner cannot comment on other cases and the only case the Examiner can comment is the case on hand. Further, both having and comprising are open-ended terms and open the claims to recited additional unrecited amino acids to either side or both sides of the amino acid sequence. Regarding BenMohammed et al teachings, Examiner noted that the extend studies used herpes and cytomegalovirus lipopeptides while the instant application uses lipid tailed polypeptides derive from the P. faliciparum. There for the BenMohammed et al teachings about herpes and cytomegalovirus lipopeptides are not the same as the lipopeptides of the case at hand.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States

11. Claims 26-40 are rejected under 35 U.S.C. 102(b) as being anticipated by Perlaza et al (July 1998), of record, as is evidenced by BenMohamed et al ((Eur. J. Immunol. 2002, 32:2274-2281), newly cited.

Perlaza *et al* teach a composition comprising LSA1-J (the instant claimed SEQ ID NO: 3) and LSA-3 NRII (the instant claimed SEQ ID NO: 2) lipopeptides in PBS (the entire document and page 3424, table I in particular), as recited in claims 26, 30, 29 and 33, wherein the lipopeptide is tailed with a lipid component (page 3423, paragraph 1 right column in particular), as recited in claims 27 and 31.

Perlaza *et al.*, further teach a vaccine composition of lipid-tailed peptides injected in phosphate-buffered saline without an adjuvant were used to immunized monkeys (in vivo) to develop an immune response (page 3423, paragraph 1 right column in particular), as recited in claims 28 and 32. The immune response was demonstrated by the induction of both B and T cell response to the peptides (page 3423, see the Abstract in particular). Further, Perlaza et al teach that the immunization with SEQ ID NO:2 and 3 is against malaria

Claim 34 is included because, while the prior art disclosure is silent as to the "the immune systemic response is a systemic B and T cell response specific to said peptide and wherein the immune systemic response is stronger than immune systemic response induced when said peptide is administered by parenteral route" per se; the product used is the same as the product of claimed invention. Therefore, the immune systemic response is a systemic B and T cell response specific to said peptide and wherein the immune systemic response is stronger than immune systemic response induced when said peptide is administered by parenteral route is considered an inherent property.

Claims 35, 36, 38 and 39 are included because the determination of the specific route of administration is well within the purview of one of ordinary skill in the art at the time the invention was made and lends no patentable import to the claimed invention. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454.456.105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

Further, as is evidenced by BenMohamed et al, that intranasal or sub-lingual delivery of malaria palmitoyl-tailed peptides without adjuvant induces strong systemic immune responses that is significantly higher than those were delivered by the subcutaneous route (see abstract in particular).

The reference teachings anticipate the claimed invention.

Applicant's arguments, filed on 5-5-03, (Paper No. 25) have been fully considered but are not persuasive.

Applicant submits that the novelty of the invention resides in the fact that a peptide having a lipid tail is imparted with an ability to cross the mucous membrane. Applicant argues that contends that in contrast to the inventive formulation of the lipopeptidic composition, peptides alone cannot cross the mucous membrane. Applicant submits that the importance of the claimed composition is not the capability to induce a protection, but the fact that it is able to induce a strong immune systemic response by simply depositing it on the oral, or nasal membrane. Applicant submits that the commonly employed delivery method of using a syringe and needle may be replaced. Applicant urges that Perlaza *et al* do not disclose a composition consisting essentially of lipid-tailed peptides to induce a strong systemic immune response when administered by mucosal route as does the claimed composition. Applicant disagrees with the Examiner statement that "Products of identical chemical composition cannot have mutually exclusive properties". Applicant provides a proof of the distinction between the properties of the composition of Perlaza et al and the present invention by comparison between various administration routes of the same chemical composition. Applicant asserts that same lipid-tailed peptides have not always the same properties (quantitative and qualitative differences in inducing systemic immune response) and it is these properties, which are present in claims 26 and 30 which clearly distinguish the claimed invention from that of Peralza et al. Applicant further argues that neither the quantitative response nor the qualitative response are the same. Applicant admits that Perlaza et al teach the recited lipid-tailed peptides of the invention, however Applicant contends that Perlaza et al do not teach any composition to induce systemic immune response when administered mucosally. Applicant asserts in Perlaza et al article, the only reference to an administration route is found in page 1, column, which only refers to subcutaneous immunizations, as well as a footnote in Table 1 that specifies that lipopeptides were "injected". Applicant agues that a reference to anticipate an invention, the reference "must teach every element of the claim".

As pointed previously and herein, Perlaza *et al.*, teach the lipopeptides of SEQ ID NO:2 and 3. Applicant has not provided objective evidence to distinguish the prior art lipopeptides from that encompassed by the claimed invention.

In contrast to applicant's assertions and as pointed out previously; when a claim recites using an old composition or structure (e.g. SEQ ID NO: 2 and SEQ ID NO: 3) is directed to a result or property of that composition or structure (e.g. inducing an immune systemic response specific to said sequence when administered via a mucosal route without adjuvant), then the claim is anticipated. See MPEP 2112.02. Also, see Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc. 58 USPQ2d 1508 (CA FC 2001); Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

In response to Applicant argument the Perlaza et al do teach a composition consisting essentially of lipid-tailed peptides to induce a strong systemic immune response when administered by mucosal route. Even though applicant has identified the administration route by which the claimed composition of the lipid-tailed peptides induce a strong systemic immune response does not appear to distinguish the prior art teaching the same product. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

In response to applicant disagreement on the Examiner position that products of identical chemical composition cannot have mutually exclusive properties. Again a chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. Further, it seems that applicant arguments are directed to the results of specific administration routes of the claimed composition rather than to the actual chemical properties of the claimed composition. Again, Perlaza et al composition is the same as the claimed composition which both have the same properties and both are capable of inducing an immune systemic response specific to the same composition when administered via a mucosal route without adjuvant as is evidenced by BenMohamed et al.

While Perlaza et al reference does not teach that the claimed composition induces systemic immune response when administered mucosally, however such property is inherent property of the claimed composition. Further, the determination of the specific route of administration is well within the purview of one of ordinary skill in the art at the time the invention was made and lends no patentable import to the claimed invention. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

Also, as restated in the court in Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999). "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art... However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. " The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art".

12. No claim allowed

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Maher Haddad, Ph.D.
Patent Examiner
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July 25, 2003

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